UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,092	10/14/2003	Karen W. Shannon	10030468-1	6820

22878 7590 02/22/2008

AGILENT TECHNOLOGIES INC.
INTELLECTUAL PROPERTY ADMINISTRATION,LEGAL DEPT.
MS BLDG. E P.O. BOX 7599
LOVELAND, CO 80537

EXAMINER	
WHALEY, PABLO S	
ART UNIT	**PAPER NUMBER**
1631	

NOTIFICATION DATE	DELIVERY MODE
02/22/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com

Office Action Summary	Application No.	Applicant(s)	
	10/686,092	SHANNON, KAREN W.	
	Examiner	Art Unit	
	Pablo Whaley	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-16 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-16 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims under Examination

Claims herein under examination are claims 1-4, 6-16 and 26-30. Claims 17-25 have been cancelled.

Withdrawn Rejections

The rejection of claims 1-4, 6-16, and 26-30 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendments filed 11/2/2007.

The rejection of claims 1, 2, 6-10, 12-16, and 26-30 under 35 U.S.C. 103(a) as being made obvious by Li et al. (Bioinformatics, 2001, Vol. 17, No. 11, p.1067-1076), in view of Ben-dor et al. (Journal of Computational Biology, 1999, Vol. 6, No. ¾, p. 281-297) is withdrawn in view of applicant's amendments and arguments filed 11/2/2007.

The rejection of claims 1-4, 7-9, 13-16, and 26-30 are rejected under 35 U.S.C. 103(a) as being made obvious by Sung et al. (Proceedings of the Computational Systems Bioinformatics (CSB'03), 11-14 August 2003, p.1-10), in view of Ben-dor et al. (Journal of Computational Biology, 1999, Vol. 6, No. ¾, p. 281-297)) is withdrawn in view of applicant's amendments and arguments filed 11/2/2007.

The rejection of claims 10 and 11 under 35 U.S.C. 103(a) as being made obvious by Li et al. (Bioinformatics, 2001, Vol. 17, No. 11, p.1067-1076), in view of Ben-dor et al. (Journal of Computational Biology, 1999, Vol. 6, No. ¾, p. 281-297), as applied to claims 1, 2, 6-10, 12-16, and 26-30, above, and further in view of Cao et al. (Cross Comparison of DNA Microarray Platforms, Alliance for Cellular Signaling Laboratories, Sept. 26, 2003, p.1-23) is withdrawn in view of applicant's amendments and arguments filed 11/2/2007.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 and 6-16 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. These claims are rejected for the following reasons. ***This rejection is newly applied.***

Claims 1-4 and 6-16 are drawn to a method of identifying a sequence of a nucleic acid. For a process to be statutory, it must provide: (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)]. As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result. The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to a process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility.

In the instant case, the claimed process does not result in a physical transformation of matter. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and useful result (i.e. a specific and substantial). Claims 1-4 and 6-16 as a whole result in "identifying any sequences of nucleic acids that are suitable for use as...normalization probes." This is not a tangible result because

merely "identifying" probes does not communicate a result in a user readable format. Therefore the claimed method does not recite a practical application of a 35 U.S.C. 101 Judicial exception and is not statutory.

This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment. For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV. The applicants are cautioned against introduction of new matter in an amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 6-10, 12-16, and 26-30 are rejected under 35 U.S.C. 103(a) as being made obvious by Li et al. (Bioinformatics, 2001, Vol. 17, No. 11, p.1067-1076), in view of Relogio et al. (Nucleic Acids Research, 2002, Vol. 30, No. 11, p.1-10) and Ben-dor et al. (Journal of Computational Biology, 1999, Vol. 6, No. ¾, p. 281-297). ***This rejection is newly applied.***

Li et al. teach a computer-implemented method and program called "ProbeSelect" for selecting an optimal number of DNA oligos for gene expression arrays. Identification and selection of candidate probes is based on selection criteria [Abstract, Fig. 2, and Table 1] based on frequency matching [p.1070, Col. 2, ¶ 2], free energy calculation [p.1071, Col. 1, ¶ 3], and sequence matching (and mismatching) [p.1071, Col. 1, ¶ 2], which are teachings for selection based on base composition and lack of homology, as in claims 1, 2, 26, and 27 (ii and iii). It is noted that selection of mismatch sequences is interpreted as a teaching for 'lack of homology, as in claims 2 and 27 (step iii). Selection criteria directed to frequency calculation [p.1071, Col. 1, ¶1] and free energy calculation [p.1072, Col. 1, ¶1] and [Table 4], are teachings for empirical evaluation as in claims 1 and 26. Candidate probes are evaluated using three different model organisms (i.e. experimental conditions), including *E. coli* bacterial cell lines [p.1074, Col. 1, ¶1], as in claims 1, 6, 12, and 26. The "ProbeSelect" computer program as described equates to a computational analysis system [p.1069, Col. 2, ¶3], as in claims 14, 15, 16, and 30. Optimal probes are output to a user [Table 1 and 2], as in claim 26 (steps e and f). Li et al. also teach subjecting arrays to experimental conditions for producing gene expression data [p.1067, Col. 2, DNA chips].

Li et al. does not specifically teach a step for empirically evaluating candidate probes, as in claims 1 and 26, step b. Li et al. does not specifically teach limitations directed to evaluating gene expression data based on clustering, as in claims 1 and 26 (step c and d), and claims 7, 8, 9, 13, 26, 28, and 29.

Relogio et al. teaches empirical methods for evaluating microarray data under different experimental conditions and obtaining empirical data for probe sensitivity, specificity, and dynamic range [See

Abstract, Fig. 1 and 2, Table 1 and 2]. Relogio also shows their methods assist in the design of DNA microarrays [p.8, Discussion].

Ben-dor et al. teach methods for analyzing gene expression patterns using clustering algorithms [Abstract]. More specifically, steps of analysis include determination of the gene expression data (i.e. expression vector) and representing data by a real-valued expression matrix comprising a measured expression level of gene *i* in experimental (condition) *j*, deriving a similarity matrix, clustering genes based on the similarity data or on the expression data [p.282, ¶3], and displaying results [p.291, Fig. A-C], as in claims 1 (step c), 7, 26 (step c, e, and f), and 28. The cluster algorithm also provides for evaluation of matching data and "negative" matching candidate probe data [p.288, lines 5-10], which is interpreted as a teaching for probes not among said clustered probes, as in claims 1 and 26 (step d), and Jaccard coefficient evaluation wherein unmatched data is not analyzed [p.288, lines 7-10], as in claim 13. Ben-dor et al. also teach clustering of candidate with substantially the same expression patterns [p.291, Fig. A and B] and use of affinity thresholds [p.291, ¶2], as in claims 8, 9, and 29.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the optimal array probe selection method of Li et al. and test these probes using the empirical evaluation methods shown by Relogio in order to assist in the selection for optimal probes using on the DNA microarrays [Relogio, p.8, Discussion]. It would further have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the optimal array probe selection method of Li et al using the clustering method of Ben-dor et al. to rapidly analyze gene expression data produced by candidate probes, since Ben-dor shows applications of their method specifically with microarray gene expression data [p.292, Section 4.2]. One of ordinary skill in the art would have been motivated to combine the probe selection method of Li and the clustering method of Ben-dor in order to provide additional information for ensuring selection of optimal probes [Li et al., p.1076, Col. 1, ¶1], or to give meaning to non-temporal gene expression data and single out conditions that have the largest effect on a

cluster based on the analysis of gene expression data , as suggested by Ben-dor et al. [p.292 and 293, Section 4.2].

Claims 1-4, 7-9, 13-16, and 26-30 are rejected under 35 U.S.C. 103(a) as being made obvious by Sung et al. (Proceedings of the Computational Systems Bioinformatics (CSB'03), 11-14 August 2003, p.1-10), in view of Relogio et al. (Nucleic Acids Research, 2002, Vol. 30, No. 11, p.1-10) and Ben-dor et al. (Journal of Computational Biology, 1999, Vol. 6, No. ¾, p. 281-297). ***This rejection is newly applied.***

Sung et al. teach a computer-implemented method for designing probes for microarrays [Abstract]. Sung shows identifying probes using a program (i.e. FindProbe), wherein three types of selection criteria are used [Section 2.1 and 2.2] including homogeneity (i.e. base content), proximity to 3' end of probes [Section 4: Sensitivity filtering], and matching and mismatching of sequences (i.e. lack of homology) [Section 5.2], as in claims 1, 2, 3, and 27. It is noted that sensitivity filtering reduced probes that form secondary structures (i.e. overlap) [Section 4], and therefore has been broadly interpreted as a teaching for minimization of candidate probes that overlap with each other, as in claim 4. Sung also shows evaluating their method of probe selection based on experimental results [Section 1.2, ¶4] and experimentally evaluating candidate probes in different experimental conditions [p.7, Section 6, Col. 1, andTable 2 and 5] as in claims 1 and 26 (step b). The "FindProbe" program is a teaching for a computational system, as in claims 14-16 and 30.

Sung et al. does not specifically teach producing empirical gene expression data, as in claim 1 (step b). Sung et al. also does not specifically teach limitations directed to clustering sequences into groups, as in claims 1 (steps c and d) and 26, and claims 7, 8, 9, 13, 26, 28, and 29.

Relogio et al. teaches empirical methods for evaluating microarray data under different experimental conditions and obtaining empirical data for probe sensitivity, specificity, and dynamic range [See Abstract, Fig. 1 and 2, Table 1 and 2]. Relogio also shows their methods assist in the design of DNA microarrays [p.8, Discussion].

Ben-dor et al. teach methods for analyzing gene expression patterns using clustering algorithms [Abstract]. More specifically, steps of analysis include determination of the gene expression data (i.e. expression vector) and representing data by a real-valued expression matrix comprising a measured expression level of gene *i* in experimental (condition) *j*, deriving a similarity matrix, clustering genes based on the similarity data or on the expression data [p.282, ¶3], and displaying results [p.291, Fig. A-C], as in claims 1 (step c), 7, 26 (step c, e, and f), and 28. The cluster algorithm also provides for evaluation of matching data and "negative" matching candidate probe data [p.288, lines 5-10], which is interpreted as a teaching for probes not among said clustered probes, as in claims 1 and 26 (step d), and Jaccard coefficient evaluation wherein unmatched data is not analyzed [p.288, lines 7-10], as in claim 13. Ben-dor et al. also teach clustering of candidate with substantially the same expression patterns [p.291, Fig. A and B] and use of affinity thresholds [p.291, ¶2], as in claims 8, 9, and 29.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the probe selection method of Sung et al. and test candidate probes using the empirical evaluation methods shown by Relogio in order to assist in the selection for optimal probes using on the DNA microarrays, as suggested by Relogio [p.8, Discussion]. It would further have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the probe selection method of Sung et al using the clustering method of Ben-dor et al. to rapidly analyze gene expression data produced by candidate probes and ensure that all candidate probes produce the expected expression patterns [Ben-dor et al., Abstract], resulting in the practice of the instant claimed invention.

Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being made obvious by Li et al. (Bioinformatics, 2001, Vol. 17, No. 11, p.1067-1076), in view of Relogio et al. (Nucleic Acids Research, 2002, Vol. 30, No. 11, p.1-10) and Ben-dor et al. (Journal of Computational Biology, 1999, Vol. 6, No. ¾, p. 281-297). , as applied to claims 1, 2, 6-10, 12-16, and 26-30, above, and further in view of Cao et al. (Cross Comparison of DNA Microarray Platforms, Alliance for Cellular Signaling Laboratories, Sept. 26, 2003, p.1-23). ***This rejection is newly applied.***

Li et al., Relogio,and Ben-dor et al. make obvious a method for selecting an optimal number of probes for use in gene expression arrays, as set forth above and applied to claims 1, 2, 6-10, 12-16, and 26-30.

Li et al, Relogio, and Ben-dor et al. do not specifically teach log-ratio limitation as in claims 10 and 11. However, Ben-dor et al. clearly teach and suggest the calculation of log-ratios of intensities [p.292, ¶ 1].

Cao et al. teach a method for comparing the reproducibility and sensitivity of several microarray platforms, including the Affymetrix GeneChip, custom cDNA arrays, and custom oligo arrays [Abstract]. More specifically, Cao et al. teach calculation of "log-ratio" values across a number of different experimental conditions [p.8] and values in the range of –0.16 to 0.44 [p.10], as in claims 10 and 11.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the probe selection method made obvious by Li, Relogio, and Ben-dor in combination with the log-ratio calculations taught by Cao et al., since Ben-dor et al. suggests the assessment of probes by taking the log-ratio of probe intensities [p.292, ¶ 1]. One of ordinary skill in the art would have been motivated to combine the above teachings in order to compare gene expression data for optimal probes that are selected using different platforms [Cao et al., p.6], resulting in the practice of the instant claimed invention.

Response to Arguments

Applicant's arguments, filed 11/02/2007, that Li and Sung fail to teach employing any empirical data in the probe selection process are moot in view of the new grounds of rejections.

Provisional Obviousness-Type Double Patenting Rejection

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *ln re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R. 1.321 (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. 3.73(b).

Claims 1-4, 6-16 and 26-30 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of co-pending Application No. 10/871,303. Although the conflicting claims are not identical, they are not patentably distinct from each

other because of the broadly encompassing scope of the instantly claimed invention causing the inventions to have overlapping embodiments. The instant claims and those of '303 recite the same method steps, with minor variations. For example, instant claims 1 and 26 are directed to methods for identifying a sequence of nucleic acid suitable for use as a normalization probe, which require evaluation of clustering and evaluation of data not in clustered data, whereas claims 1-11 of co-pending of '303 are directed to a method for identifying and selecting nucleic acid probes, which require selecting probes, forming of clusters based on hybridization data, and identifying clusters not in a Supercluster. Therefore, It would have been obvious to someone of ordinary skill in the art at the time of the instant invention evaluate Superclusters and data not in superclusters, as evaluating cluster gene expression data and hybridization data are well-known in the art. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's request, filed 11/2/2007, that this rejection be held in abeyance until allowance of claims in the instant application is acknowledged. However, this rejection will not be withdrawn until a Terminal Disclaimer is filed by applicant and approved by the Office. This rejection is therefore maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Pablo S. Whaley/

Patent Examiner

Art Unit 1631

/John S. Brusca/

Primary Examiner, Art Unit 1631